REMARKS

Claims 1, 6, 8, 9, 11, 13, 17, 19, 22, 26, 27, 31, 36 and 43 are pending in the subject application. By this Amendment, applicants have canceled claims 1, 6, 8, 11, 13, 17, 19, 22, 26, 27, 31, 36 and 43 without disclaimer or prejudice to applicants' rights to pursue the subject matter of this claim in this or in a later application. Applicants have also amended claim 9. Applicants maintain that claim 9, as amended, is fully supported in the specification at, *inter alia*, page 15, lines 14-16; page 20, lines 13-14; page 63, lines 3-9; and page 72, lines 3-33. Thus, the claim amendments do not raise any issue of new matter. Accordingly, applicants respectfully request that the Examiner enter this Amendment. Upon entry of this Amendment, claim 9, as amended herein, will be pending and under examination.

Election/Restrictions

The Examiner stated that applicants' November 22, 2004 traversal of the restriction requirement is not found to be persuasive. Accordingly, the Examiner stated that the requirement is still deemed proper and is therefore made FINAL.

In response, applicants have canceled, without disclaimer or prejudice, claims 1, 6, 8, 11, 13, 17, 19, 22, 26, 27, 31, 36 and 43 which were withdrawn by the Examiner as being drawn to a non-elected invention.

Sequence Compliance

The Examiner stated that this application contains sequence disclosures in Fig. 4 and in Table 4 on page 45 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). The

Examiner stated that this application, however, fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825 for the reason(s) set forth in a Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures which was supposedly attached to the Office Action.

The Examiner requested that applicants identify the sequence identification numbers (SEQ ID NOs.) for the disclosed sequences listed above for full compliance with the sequence rules in response to the Office Action. The Examiner also stated that a complete response to the Office Action should include both compliance with the sequence rules and a response to the Office Action set forth below.

In response, applicants note that no Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures was attached to the March 23, 2005 Office Action received by applicants, and no such Notice has been posted on the Patent Office's public PAIR site. Therefore, applicants are uncertain exactly what is required to comply with the Notice that has not been issued.

From the Examiner's remarks, applicants understand that the sole problem may be that the Sequence Listing filed on July 23, 2002 did not contain the sequences disclosed in Figure 4 and in Table 4 on page 45. Accordingly, applicants intend to contact the Examiner as soon as possible to confirm that this is all that is required, and will then promptly file a Supplemental Response.

Priority Claims

The Examiner acknowledged applicants' claim for domestic priority of Provisional Application No. 60/019,941, filed on June 14, 1996

under 35 U.S.C. §119(e). However, the Examiner stated that the benefit to the earlier filing date of this provisional application is denied because the provision application lacks an adequately enabled description that supports pending claim 9 under 35 U.S.C. §112. In this regard, the Examiner also stated that the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. §112 (citing *Transco Products, Inc.* v. *Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994)).

The Examiner further stated that in the instant case, after carefully reviewing the provision application, she found that the provisional application only has 39 pages in content, 1 series of experiments and 3 Figures, which only disclose that β-chemokines, native ligands of CC-CKR5 (CCR5 synonym), can inhibit macrophage-tropic HIV-1 infection. The Examiner additionally stated that there is, however, no enabling disclosure of any CCR5 antibody except for one sentence of a superficial description: "This invention provides an antibody or a portion thereof capable of binding to a chemokine receptor on a $CD4^+$ cell and inhibiting HIV-1 infection of the cell" (citing page 12, lines 10-13; and claim 7).

The Examiner asserted that there is no disclosure of a method of making or of using the antibody. The Examiner also asserted that it was not until the parental application, 09/874,618, was filed that an example that describes an anti-CCR5 antibody was included in the specification. The Examiner further pointed out that the subject application and the parent application, 08/874,618, contain a new portion and disclosure from pages 40 to 81, including 10 more figures and three more series of experiments, including an enabling disclosure of a CCR5 antibody.

In addition, the Examiner acknowledged applicants' claim for domestic priority of non-provision application 08/874,618, filed June 13, 1997, under 35 U.S.C. §120. The Examiner also stated that because application 08/874,618 has the same content as the subject application, the priority date of the subject application is considered to be the filing date of the parent application, 08/874,618, but not the June 14, 1996 filing date of Provisional Application No. 60/019,941.

In response, applicants respectfully traverse the Examiner's denial of the benefit of the June 14, 1996 filing date of Provisional Application No. 60/019,941. Applicants note that by the June 14, 1996 filing date of this provisional application, the CCR5 receptor gene had been cloned and the receptor functionally expressed in a stably transfected mammalian cell line. See, for example, Samson et al. (1996) Molecular cloning and functional expression of a new human CC-chemokine receptor gene, Biochemistry: 3362-3367 (published March 19, 1996). Applicants also note that by June 14, 1996, the making of monoclonal antibodies directed against the product of a cloned gene expressed on a cell surface was routine in the art. See Kohler and Milstein (1975) Continuous cultures of fused cells secreting antibody of predefined specificity, Nature 256: 495-497. Thus, applicants maintain that the disclosure of "an antibody or a portion thereof capable of binding to a chemokine receptor on a $CD4^+$ cell and inhibiting HIV-1 infection of the cell" in Provisional Application No. 60/019,941 is enabled since, based on this disclosure, one of ordinary skill in the art could make the disclosed antibody. Applicants note also that, contrary to the Examiner's assertion, the specification of Application No. 60/019,941 discloses a use of the antibody in treating an HIV-infected subject (see page 3, lines 18-21).

Applicants therefore maintain that the disclosure of the claimed

invention in Provisional Application No. 60/019,941 is sufficient to comply with the enablement requirements of 35 U.S.C. §112, first paragraph, and hence the pending claim is entitled to the benefit of the filing date of this provisional application. Accordingly, applicants respectfully request that the Examiner withdraw the denial of the benefit of the June 14, 1996 filing date of Application No. 60/019,941 to the subject application.

Rejection under 35 U.S.C. §101

The Examiner rejected claim 9 under 35 U.S.C. §101 as allegedly directed to non-statutory subject matter. The Examiner stated that the claimed antibody reads on naturally occurring material, which is considered to be non-statutory and non-patentable subject matter within the scope of 35 U.S.C. §101 (citing Official Gazette, 1077 O.G. April 21, 1987). The Examiner also advised that amending the claim to incorporate "[an] isolated or purified" in front of "antibody or portion of antibody" would overcome this rejection.

In response, applicants note that claim 9, as amended herein, refers to "[a]n isolated or purified antibody or a portion of such an antibody..." Accordingly, applicants respectfully request that the Examiner withdraw this ground of rejection.

Obviousness-type Double Patenting Rejections

The Examiner provisionally rejected claim 9 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 98-134 of copending Application No. 09/594,983. The Examiner stated that although the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of the conflicting claims overlap.

The Examiner also provisionally rejected claim 9 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-5 of copending Application No. 10/371,483. The Examiner stated that although the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of the conflicting claims overlap.

The Examiner further provisionally rejected claim 9 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 15-17 of copending Application No. 09/412,284. The Examiner stated that although the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of the conflicting claims overlap.

The Examiner also provisionally rejected claim 9 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 51-56 of copending Application No. 09/888,938. The Examiner stated that whereas the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of the conflicting claims overlap.

In response, applicants respectfully traverse these obviousness-type double patenting rejections. Nevertheless, without conceding the correctness of the Examiner's position, applicants will consider filing a terminal disclaimer if the claim under examination is otherwise allowable.

Rejections under 35 U.S.C. §102

35 U.S.C. §102(a)

The Examiner rejected claim 9 under 35 U.S.C. §102(a) as allegedly anticipated by Wu et al. (J. Exp. Med., May 5, 1997, pp. 1681-1691; henceforth "Wu-1"). According to the Examiner, Wu-1 teaches the isolation of several anti-CCR5 monoclonal antibodies designated 3A9, 5C7, 2F9, 3D8, 2C4, 5D7, 5H11 and HG4 (citing page 1683, last paragraph of the first column). The Examiner stated that Wu-1 particularly demonstrates that the antibody 3A9 competes with native chemokine ligands of CCR5 for binding to CCR5 (citing page 1683, first paragraph of Results, and Figs. 5 and 6 on page 1687), and inhibits macrophage-tropic HIV infection on peripheral blood mononuclear cells (citing Fig. 6 on page 1687). The Examiner asserted that the claimed invention is therefore anticipated by Wu-1.

In response, applicants respectfully traverse this rejection. Without conceding the correctness of the Examiner's position, applicants note that claim 9, as amended herein, is directed to an isolated or purified antibody or a portion of such an antibody capable of (1) binding to the second extracellular loop (ECL2) of a CCR5 chemokine receptor on a $CD4^+$ cell and inhibiting fusion of HIV-1 to, and thereby HIV-1 infection of, the $CD4^+$ cell, and (2) blocking binding of a sCD4:gp120 complex to a CCR5 receptor on the surface of such $CD4^+$ cell. Applicant asserts that there is no teaching in Wu-1 that any of the disclosed anti-CCR5 monoclonal antibodies is capable of (1) binding to the ECL2 of a CCR5 chemokine receptor on a $CD4^+$ cell, or (2) blocking binding of a sCD4:gp120 complex to a CCR5 receptor on the surface of a $CD4^+$ cell.

Applicants note that a finding of anticipation requires that a

prior art reference teach each and every element of the rejected claims. Since Wu-1 does not teach an antibody which is capable of binding to the ECL2 of a CCR5 chemokine receptor on a $CD4^+$ cell, or of blocking binding of a sCD4:gp120 complex to a CCR5 receptor on the surface of a $CD4^+$ cell, applicants maintain that claim 9, as amended, is not anticipated by Wu-1.

In addition, applicants assert that they completed the conception of an anti-CCR5 antibody having the properties recited in claim 9, as amended herein, prior to the May 5, 1997 publication of Wu-1, and were diligent in reducing this invention to practice from a time just prior to May 5, 1997 until the June 13, 1997 filing date of the subject application. Accordingly, applicants intend to file at a later date a Declaration under 37 C.F.R. 1.131 providing evidence of the invention of the subject matter of claim 9 prior to the May 5, 1997 publication date of Wu-1.

35 U.S.C. §102(e)

The Examiner rejected claim 9 under 35 U.S.C. §102(e) as allegedly anticipated by Littman et al., U.S. Serial No. 5,939,320 A ("Littman A") or Littman et al., U.S. Serial No. 6,258,527 B1 ("Littman B"). The Examiner stated that Littman et al. A or B teach that CC-CKR5 (synonym of CCR5) is a fusion cofactor for macrophage-tropic (M-tropic) HIV. The Examiner also stated that Littman et al. designate this receptor a HIV translocation promoting agent that acts in conjunction with CD4 to facilitate the HIV-1 macrophage envelope protein-mediated fusion and penetration into the target cell to establish HIV infection (citing col. 2, lines 38-65). The Examiner stated that Littman et al. further teach that such an antibody can bind to CC-CKR5 and block the M-tropic envelope of HIV-1 mediated fusion and infection (Littman A: col. 20, line 19 through to col. 24, line 37; or Littman B: col. 22, line 36 through to col. 27, line

45). The Examiner concluded that Littman A or Littman B therefore anticipates the claim.

The Examiner also stated that the priority date of the Littman et al. patents is based on the earlier May 20, 1996 filing date of U.S. Provisional Application No. 60,017,157, since this provisional application has a disclosure of an antibody against CC CKR5 (citing claims 1 and 7-12, and the entire document).

In response, applicants respectfully traverse the above rejection. Without conceding the correctness of the Examiner's position, applicants note again that claim 9, as amended herein, is directed to an isolated or purified antibody or a portion of such an antibody capable of (1) binding to the second extracellular loop (ECL2) of a CCR5 chemokine receptor on a $CD4^+$ cell and inhibiting fusion of HIV-1 to, and thereby HIV-1 infection of, the $CD4^+$ cell, and (2) blocking binding of a sCD4:gp120 complex to a CCR5 receptor on the surface of such $CD4^+$ cell.

Applicant notes that Littman A and Littman B were filed June 19, 1996 and May 21, 1997, respectively, and are each continuation-in-part applications of U.S. Provisional Application No. 60/017,157, filed May 20, 1996. Thus, to be available as prior art against the claimed invention, Littman B must be entitled to the benefit of the May 20, 1996 filing date of Provisional Application No. 60/017,157. Applicants note that whereas, as the Examiner noted, Littman A and B teach an anti-CCR5 antibody that blocks HIV-1 binding (see, e.g., Littman B: col. 7, lines 17-18), Application No. 60/017,157 does not disclose such an antibody. Thus, with regard to an anti-CCR5 antibody that inhibits fusion of HIV-1 to, and thereby HIV-1 infection of, a $CD4^+$ cell, applicants maintain that Littman B is not entitled to a May 20, 1996 effective date, and therefore is not prior art against the

subject application.

Moreover, applicants assert that there is no teaching in Littman A or B of an anti-CCR5 monoclonal antibody that is capable of (1) binding to the ECL2 of a CCR5 chemokine receptor on a $CD4^+$ cell, or (2) blocking binding of a sCD4:gp120 complex to a CCR5 receptor on the surface of a $CD4^+$ cell.

Applicants reiterate that a finding of anticipation requires that a prior art reference teach each and every element of the rejected claims. Applicants therefore maintain that claim 9, as amended, is not anticipated by Littman A, since this patent does not teach an antibody which is capable of binding to the ECL2 of a CCR5 chemokine receptor on a $CD4^+$ cell, or of blocking binding of a sCD4:gp120 complex to a CCR5 receptor on the surface of a $CD4^+$ cell.

As noted above, applicants maintain that Littman B is not a prior art reference against the subject application. However, even if it were a prior art reference, applicants maintain that it would not anticipate claim 9, since it too does not teach an antibody which is capable of binding to the ECL2 of a CCR5 chemokine receptor on a $CD4^+$ cell, or of blocking binding of a sCD4:gp120 complex to a CCR5 receptor on the surface of a $CD4^+$ cell.

The Examiner also rejected claim 9 under 35 U.S.C. §102(e) as allegedly anticipated by Wu et al., U.S. Patent No. 6,528,625 B1 ("Wu-2). The Examiner stated that Wu-2 discloses an isolated anti-CCR5 monoclonal antibody or fragment thereof, including monoclonal antibody 2D7 and 5C7, wherein the monoclonal antibody 2D7 is able to bind to the second loop of CCR5, inhibit the binding of HIV-1 gp120 to CCR5 on the target cell, and block the entry of a wide range of M-tropic and dual-tropic HIV isolates into the target cells (citing col. 37, line 51 through to col.

40, line 63). The Examiner concluded that Wu-2 therefore anticipates the claimed invention.

In response, applicants respectfully traverse this rejection. Applicant asserts that there is no teaching in Wu-2 of an anti-CCR5 monoclonal antibodies that blocks binding of a sCD4:gp120 complex to a CCR5 receptor on the surface of a $CD4^+$ cell. Since Wu-2 does not teach the element of the claimed invention, applicants maintain that claim 9, as amended, is not anticipated by Wu-2.

Conclusion

In view of the remarks presented above, applicants respectfully request that the Examiner reconsider and withdraw the claim rejections set forth in the September 23, 2005 Office Action. Applicants maintain that claim 9, as amended, the sole claim pending, is in condition for allowance. Accordingly, applicants earnestly solicit allowance of this claim.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $510.00 fee for a three-month extension of time is deemed necessary in connection with the filing of this Amendment. However, if an additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

John P. White
Registration No. 28,678
Attorney for Applicants
Cooper & Dunham, LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

9/23/05

John P. White
Reg. No. 28,678

Date